REMARKS

This paper is filed in response to the Office Action, mailed April 07, 2005. A response to the Office Action was due on July 07, 2005. Applicant is filing this response with a three-month extension of time, therefore, this response, filed on or before October 7, 20054, is to be considered timely.

Claims 1-26 are pending in the application. Claims 1-26 have been rejected Claims 3 and 26 have been canceled. Claims 1, 4-7, 13-15 and 18 have been amended. No new subject matter has been added to the subject application with the filing of this amendment. Applicants reserve their right to file continuation applications on the subject matter from the canceled claims.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner maintained that claims 1-26 were rejected under §112, first paragraph, because the specification, while being enabling for the treatment of neuoroblastoma, glioblastoma and rhabdomyosarcoma, does not reasonably provide enablement for the treatment of all types cancer using the claimed compounds. In support of this position, the Examiner cited **In re Wands**, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicant respectfully traverses this rejection and provides the following comments.

In response, applicant respectfully states that per the **Wands** factors, that applicant has enabled the claims to treat cancer. With regard to the state of prior art, applicant respectfully points out as per the first page of applicants specification and the Examiner's own references, that the claimed compounds have an effect on a number of cancers. Burton shows the anti-tumor effect of tumor DNA of irinotecan (see Burton, page 3, middle two paragraphs). Applicant respectfully suggests that cancers other than those specified by the Examiner can be treated by these compounds due to general cytotoxic chemotherapeutic action they inflict on tumor DNA. Therefore, these compounds are enabled by the art and the specification to treat cancer. In support of this, applicants refer the Examiner to the references cited on page 1 of the specification. Applicant suggests that the examples provided in the specification on pages 7-24, in addition to the general knowledge in the art, provide ample support to alleviate the burden of undue experimentation to one of ordinary skill in the art.

Thus contrary to the Examiner's rejection, applicants suggest that the combination of the two compounds, as claimed herein are enabled to treat cancer and therefore, applicants respectfully request the withdrawal of this rejection.

New Rejection under 35 U.S.C. §103(a)

Claims 1-25 were newly rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 97/12630 in view of Ragab U.S. 6,346,524, Burton et al. and Friedman. The Examiner stated that Burton et al. discuss new chemotherapy options for patients suffering gliomas, in particular the use of temozolomide and irinotecan. The Examiner stated that single dosing of temozolomide and irinotecan had been demonstrated by Burton be effective in certain cancer treatments. The Examiner stated that Ragab demonstrated administering an effective amount (40-150 mg/m^2/day) for a dosing period of from about 5 to 25 days to cure or eliminate cancer. The Examiner stated that Friedman teaches a method of treating cancer (gliomas, melanomas, carcinomas, sarcoma, leukemia, etc.) by use of temozolomide. Col. 10, Lines 35-65. The Examiner stated that Friedman also discloses temozolomide in combination with other chemotherapeutic agents such as irinotecan. Col. 13, lines 1-5. Additionally, Claim 26, drawn to a medical kit, was also rejected under §103.

As an initial matter, applicant has cancelled claim 26, thus mooting its rejection.

Applicants respectfully traverse the rejection and provide the following comments.

Per Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) and MPEP § 2144, the criteria for a prima facie case of obviousness are:

- Determining the scope and contents of the prior art.
- Ascertaining the differences between the prior art and the claims at issue.
- Resolving the level of ordinary skill in the pertinent art.
- Considering objective evidence in the application indicating obviousness or nonobviousness.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

Because of the differences between the scope of the prior art and the claimed invention, per the first and second Graham factors, applicant respectfully suggests that a prima facie case of obviousness cannot be established.

Applicant claims a method of treatment using therapeutically effective amounts of temozolomide in combination with irinotecan. Therapeutically effective amounts temozolomide and irinotecan are described on pages 4-6 of the specification. Applicant notes that the Examiner concedes that neither reference teaches a combination of temozolomide and irinotecan.

The Examiner references Ragab and Burton et al. for their disclosure of temozolomide and irinotecan. However, there is no teaching or suggestion in either reference to combine irinotecan in combination with temozolomide to treat cancer.

In fact, Burton et al. teaches away from the applicant's invention by the fact that it mentions both monotherapy with irinotecan AND temozolomide, but as the Examiner concedes, does not teach a combination therapy of the two compounds.

Further, Ragab merely discloses the use of temozolomide **alone**, (see generally, Abstract, col. 2, lines 31-45 and claims 1-11 of Ragab) there is no teaching or suggestion of combination therapy with irinotecan. In addition, applicant believes that one of ordinary skill in the art would not necessarily consider Ragab's mono therapy of temozolomide to treat cancer when practicing the combination temozolomide and irinotecan therapy described by the applicant's invention. Finally, neither Ragab or Burton et al. contain any teaching or suggestion to combine any of them in order to teach applicant's claimed invention, temozolomide in combination with irinotecan. Applicant respectfully suggests that per the first and second Graham factors, these differences in the scope and contents of the claimed invention from the cited art preclude a finding of obviousness.

The Examiner cites Friedman for the premise that it cites using both temozolomide and irinotecan to treat various cancer. However, Friedman is silent on applicant's amended claim 1, where temozolomide and irinotecan are administered over repeated 21 day cycles, where said 21 day cycles are divided into three 1 week periods. Furthermore, Friedman at col. 13, lines 1 to 7 limits itself to the use of microcrystalline temozolomide in combination with other chemotherapeutic agents, unlike the presently pending application.

Furthermore, the efficacy of a drug with respect to a particular disease cannot be predicted based upon treatment of that disease with a structurally and functionally distinct drug, such as irinotecan and temozolomide. Thus, one having ordinary skill in the art could not predict for irinotecan whether the total drug exposure or its peak plasma level would be important in treating cancer because temozolomide and irinotecan are different drugs. Thus, the references cited by the Examiner are not predictive of treating cancer with irinotecan and temozolomide, with the 21 day cycles, especially due to the synergistic effects stated by the specification by Example C, starting on page 7, line 20 to page 10, line 23.

Therefore, applicant respectfully submits that the claimed invention is not obvious in light of Friedman, Ragab and Burton et al. Reconsideration and withdrawal of this ground of rejection is respectfully urged.

In view of the remarks above, applicant respectfully submits that the application is in condition for allowance. Accordingly, applicant requests

reconsideration of the application, withdrawal of the rejections of record and issuance of a Notice of Allowance.

No fees, other than the appropriate extension of time fees, are due by the submission of this paper however, if any fees are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from **Account No. 19-0365.**

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Respectfully submitted,

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